

1     Claims

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1.     A method for synthesising a given peptide or its derivative which contains a proline residue or a proline derivative, at proximity to, or at, the C-terminal end of said peptide, the method comprising the steps of:

- a)     synthesising on a first resin a C-terminal portion of said peptide, or its derivative, comprising at least three successive amino acid residues or their derivatives, by successive coupling of selected amino acids, small peptides or their derivatives, said first resin being suitable for the formation of peptides having a proline residue or a proline derivative positioned at, or at proximity of, the C-terminal end of said peptide;
- b)     cleaving the C-terminal portion thus obtained from said first resin;
- c)     reattaching said C-terminal portion to a second resin which is generally suitable for the synthesis of peptides but is unsuitable for the formation of peptides having a proline residue or a proline derivative positioned at, or at proximity of, the C-terminal end of said peptide; and
- d)     coupling selected amino acids, small peptides or derivatives to the C-terminal portion to obtain said given peptide.

- 1     2.    The method of Claim 1 wherein said peptide is  
2           a long peptide.  
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- 4     3.    The method of Claim 1 or 2 wherein said given  
5           peptide is a chemokine having a proline  
6           residue or a proline derivative at the C-  
7           terminal or at proximity thereof.  
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- 9     4.    The method of any one of Claims 1 to 3,  
10          wherein said first resin is chosen so that it  
11          does not lead to the formation of cyclic  
12          dipeptide and in particular diketopiperazine  
13          compounds.  
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- 15    5.    The method of any one of Claims 1 or 4,  
16          wherein said step a) and/or d) is achieved by  
17          successive coupling of the predetermined amino  
18          acid residues or derivatives.  
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- 20    6.    The method of any one of Claims 1 to 5,  
21          wherein said first resin for the formation of  
22          the C-terminal portion is the 2-chlorotrityl  
23          chloride resin.  
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- 25    7.    The method of any one of Claims 1 to 6,  
26          wherein said second resin is a resin of the  
27          type having benzyl ester linkers.  
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- 29    8.    The method of any one of Claims 1 to 7,  
30          wherein said second resin is a Wang type  
31          resin.  
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- 1     9.    The method of any one of Claims 1 to 8,  
2            wherein said given peptide as up to 150 amino  
3            acid residues.  
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- 5     10.   The method of any one of Claims 1 to 9,  
6            wherein the cleaving step is achieved using a  
7            mild acid treatment, for example 20%  
8            trifluoroethanol in dichloromethane.  
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- 10    11.   The method of any one of Claims 1 to 10,  
11            wherein the C-terminal portion is fully  
12            protected so it can be attached directly onto  
13            the second resin.  
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